23. (Amended) The method of claim 20, further comprising (b) exposing the cell to light, whereby said light exposure promotes disaggregation of the aggregated composition.

REMARKS

Claims 8, 18, 19, 22 and 23 have been amended without prejudice. Claims 8, 19, 22 and 23 are amended to correct form or grammar. Support for the amending language of claim 18 can be found throughout the specification, specifically on page 2, lines 15-25 and on page 11, lines 8-12. No new matter has been added.

Reconsideration of the subject application is respectfully requested

Priority Claim

Applicants note the acknowledgement of the claims for priority based on priority applications GB 9930499.0, filed December 24, 1999 and GB 9905444.7 filed March 10, 1999. Certified copies of these applications have been requested, and will be submitted once obtained.

Sequence listing

Applicants submit herewith a printed "Sequence Listing," and a "Statement in Compliance with 37 C.F.R.§1.821(f)," and a computer readable form of the sequence listing. Applicants submit that the application is now in compliance with 37 C.F.R.§1.821 through 1.825.

The Office action notes that claim 3 allegedly does not comply with the Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. However, claim 3 does not currently recite an amino acid sequence, but rather refers to the specific amino acids in a protein which is identified not by sequence but by name (VP22). If the objection is maintained, Applicants respectfully request further clarification.

Claims Objections

Claim 8 was objected to as it contained a spelling error. Claim 8 has been amended, thereby removing the objection.

Rejection under 35 USC § 112, second paragraph

Claims 18, 19, 22, and 23 were rejected under 35 USC § 112, second paragraph, as allegedly omitting essential steps. Claims 18, 19, 22, and 23 were amended, thereby removing the rejection.

Rejections under 35 USC § 103

Claims 1-10 and 12-22 stand rejected as obvious over O' Hare et al.(WO 97/05265) in view of Schwartz et al. (USP 6,034,135). Applicants respectfully disagree with the rejection.

Neither O' Hare et al. nor Schwartz et al., when read either singly or in combination, mention or suggest the VP22-containing aggregates particularly specified in the present claims: these are clearly explained in the present application as "associations of molecules forming particles" (page 2, line 22) and they can be produced by mixing VP22 with oligonucleotide or polynucleotide. Nor is there any motivation apparent in these cited documents, when read either singly or in combination, to make such special VP22 aggregates.

O' Hare et al. mentions a VP22 polypeptide attached to another molecule to be transported, e.g. covalently or non-covalently attached (for example WO 97/05265 at page 5, lines 18-37). However, such molecules are not the special aggregated particles of the present invention as defined by the present claims: there is no disclosure or suggestion of aggregation in O'Hare et al.

While Schwarz et al. (USP 6,034,135) does mention certain aggregates, these are of quite different composition than those of the present claims. Thus, in contrast to the aggregates of the present invention, essentially comprising the ingredients specified in the independent claims herein, those of Schwarz et al. comprise cationic lipids which themselves aggregate with anionic macromolecules through attraction between the positively charged lipid and the negatively

charged anionic macromolecule (USP 6,034,135 at column 10, line 66 to column 11, line 10). These compositions are far removed from the aggregates between VP22 and polynucleotides or oligonucleotides claimed herein.

While dependent claim 17 of the present application does specify the presence of a liposome, this encapsulates an already-formed VP22 aggregate. Such an encapsulated VP22 aggregate is neither mentioned nor suggested in Schwarz et al.

Also, Schwarz et al. teaches away from the aggregates of the present invention as Schwarz et al provide a different type of aggregate – a cationic lipid aggregate – and the skilled person would be motivated on reading Schwarz et al. to make these cationic lipid aggregates, which would not result in compositions as claimed herein. There is no apparent motivation present in either document for the skilled person to try to make VP22 aggregates as claimed herein.

Reconsideration and withdrawal of the rejection is respectfully requested.

Claim 11 stands rejected as obvious over O' Hare et al.(WO 97/05265) in view of Schwartz et al. (USP 6,034,135) and in further view of Moyer et al. (USP 5,935,777).

Claim 11 specifies a VP22 containing aggregate in which a non-VP22 polypeptide is linked to VP22 by a cleavage-susceptible amino acid sequence.

If one of skill in the art were to read O' Hare et al. in combination with Schwartz et al. and Moyer et al. they would not produce the aggregates specified by claim 11, since (for reasons already given above) the VP22 aggregates themselves are submitted to be non-obvious in view of O' Hare et al. in combination with Schwartz et al. Moyer et al. does not relevantly add to the disclosure of the other prior art items as Moyer et al. makes no mention or suggestion of any aggregates, nor does Moyer mention or suggest VP22.

Indeed, the record gives no grounds for *prima facie* belief that the skilled person would be motivated to read Moyer in combination with O' Hare and Schwartz, since the Moyer citation is in a different field and describes novel EBV vectors for protein expression (column 3, lines 50-61).

Hence, for all of these reasons the present claims are submitted to be inventive in relation to the above citations.

Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

It is respectfully submitted that the present claims are in condition for allowance. If any issues remain to be addressed, the Examiner is respectfully requested to call the undersigned patent attorney, at the Portland telephone number listed below, to discuss those issues.

Respectfully submitted,

KLARQUIST SPARKMAN CAMPBELL
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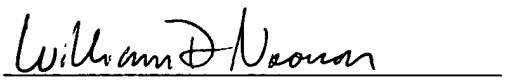
By 
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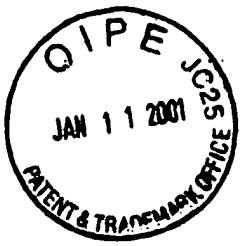

Marked-up Version of Amended Claims
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

1. (Reiterated) An aggregated composition comprising (a) a polypeptide having the transport function of VP22, and (b) an oligonucleotide or polynucleotide.

2. (Reiterated) An aggregated composition according to claim 1, which further comprises a pharmaceutically acceptable excipient.

3. (Reiterated) An aggregated composition according to claim 1, wherein the polypeptide is a VP22 fragment comprising amino acid residues 159-301 of VP22.

4. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide comprises a circular plasmid.

5. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide comprises modified phosphodiester linkages.

6. (Reiterated) An aggregated composition according to claim 5, wherein the modified phosphodiester linkages comprise phosphorothioate linkages.

7. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide is labeled with a detectable label.

8. (Amended) An aggregated composition according to claim 1, wherein the [oglionucleotide] <u>oligonucleotide</u> or polynucleotide is selected from the group consisting of: an antisense molecule, a ribozyme molecule, a chimeroplast, and a polynucleotide capable of binding a transcription factor.

9. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide encodes a protein or peptide.

10. (Reiterated) An aggregated composition according to claim 1, wherein the polypeptide is a fusion protein comprising a non-VP22 peptide or protein.

11. (Reiterated) An aggregated composition according to claim 10, wherein the non-VP22 polypeptide sequence is linked to the polypeptide having the transport function of VP22 by a cleavage-susceptible amino acid sequence.

12. (Reiterated) An aggregated composition according to claim 1, wherein the polypeptide is conjugated to a glycoside.

13. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide is coupled to a non-nucleotide molecule.

14. (Reiterated) An aggregated composition according to claim 1, wherein the aggregate comprises polypeptide and nucleotide in a ratio of at least 1 to 1.

15. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide comprises at least about 10 bases.

16. (Reiterated) An aggregated composition according to claim 1, which comprises particles of said aggregated composition having a particle size in the range of about 0.1 to about 5 microns.

17. (Reiterated) An aggregated composition according to claim 1, wherein said polypeptide and said nucleotide are encapsulated in a liposome.

18. (Amended) A method of making an aggregated composition according to claim 1 comprising, (a) [mixing] contacting [a] polypeptide with the transport function of VP22, with [the] oligonucleotide or polynucleotide, wherein said contact is in solution, then (b) mixing the solution obtained in step (a), and, [(b)] (c) [allowing] incubating the mixture obtained in step [(a)] (b) such that said incubation is sufficient for the VP22 and oligonucleotide or polynucleotide to form aggregates.

19. (Amended) A method according to claim 18, wherein the polypeptide is [mixed] contacted with nucleotide in a ratio of at least 1 to 1 of polypeptide to nucleotide.

20. (Reiterated) A method of delivering molecules to a cell in vitro comprising (a) contacting said cell with an aggregated composition according to claim 1.

21. (Reiterated) A cell preparation which as been treated with an aggregated composition according to claim 1.

22. (Amended) The method of claim 18, [wherein the] further comprising (d) isolating aggregates obtained in step (c) which have a particle size of about 0.1 to about 5 microns.

23. (Amended) The method of claim 20, further comprising (b) exposing the cell to light [to], whereby said light exposure promotes disaggregation of the aggregated composition.